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EXAMINER	
KATCHEVES, KONSTANTINA T	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,476	CHAE, YOUNG-JIN	
	Examiner	Art Unit	
	Konstantina Katcheves	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are pending in the present application.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d) on 18 February 2002 (Korean Application Number: PATENT-2001-0006587), which papers have been placed of record in the file.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirement of 37 CFR 1.821(d) requiring the use of an appropriate sequence identifier ("SEQ ID NO:"). Applicant's specification and claims refer to sequences set forth in the sequence listing. However, Applicant's sequence identifiers are not compliant with 37 CFR 1.821(d) and additionally inconsistent (e.g. "sequence ID. No." or "seq. ID. No."). Each reference to a sequence requires an appropriate sequence identifier "SEQ ID NO:" in the text of the description or claims preceding the reference to a sequence. Correction is required.

Specification

The use of the trademark Ambion™ has been noted in this application. See e.g. Specification pages 11 and 12. It should be capitalized wherever it appears and be accompanied by the generic terminology. Applicant should note that this objection relates to any improperly used trademarks that may have bee omitted by the examiner.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claims 2, 3, 7 and 8 are objected to because of the following informalities:

1. Pursuant to 37 CFR 1.75(c), a multiple dependent claim must recite the claims from which they depend in the alternative only; however, claims 3 and 8 depend on more than one claim inclusively and not in the alternative. See also MPEP 608.01(n)(B)(1).
2. Claims 2, 3, 7 and 8 recite the plural verb "comprising;" however the singular verb "comprises" is grammatically correct.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawley-Nelson et al. (US Patent No. 5,736,392).

The invention of claim 1 is broadly drawn to a peptide vector comprising a leader peptide, a linker DNA, and a desired gene. Given the breadth of the claim, the leader peptide of the claim relates to a broad genus of peptides that are linked or complexed to DNA in some way and a linker DNA may include any DNA that is associated or complexed with peptides or proteins. The invention of claim 3 is broadly drawn to a protein-DNA complex comprising a peptide of SEQ ID NO:1 and a DNA of SEQ ID NO:2 and a DNA of SEQ ID NO:3. The breadth of this claim reads on any protein-DNA complex so long as at least one peptide, at least one nucleotide of SEQ ID NO:2 and at least one nucleotide of SEQ ID NO:3 are present in the complex. The invention of claim 6 is broadly drawn to a method for introducing and expressing a gene of interest by infecting a cell with the peptide vector as described in claim 1 and as interpreted above.

Hawley-Nelson et al. disclose DNA complexed with a peptide wherein the peptide is coupled to a DNA binding group. See abstract and column 9, line 51. The DNA binding group is complexed to a specific DNA sequence, *i.e.* a linker DNA. See abstract and column 6, lines 50-52. Moreover, the peptide, RGD peptide, need not include a DNA binding group. It may associate directly with the linker DNA. See column 9, lines 58-65. This complex is used for transfection of cells and the expression of a gene of interest which is present in the complex in addition to the part of the DNA which complexes to the peptide. See column 12, line 49-54.

The gene of interest includes a marker such as ß-gal. See example 4. The RGD peptide includes glycine, arginine, serine and cysteine which are all present in SEQ ID NO:1 also because DNA is composed of nucleic acids A, T, G and C the DNA disclosed by Hawley-Nelson et al. which encodes the gene of interest and the DNA which complexes with the RGD peptide would inherently possess at least one of the nucleotides of SEQ ID NOS: 2 and 3.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vitro* methods for expression, does not reasonably provide enablement for *in vivo* methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Nature of the invention and breadth of the claims

Methods of targeting nucleic acids into host cells *in vivo* fall into the broad area of gene therapy. Successful gene therapy methods are based, fundamentally, upon the ability to deliver exogenous nucleic acids to cells or tissues of interest. The method of the present claims is drawn to a method for delivering and expressing a nucleic acid encoding a protein of interest into a cell. Given the disclosure of page 13 of the specification and the breadth of the claims, the method is drawn to *in vivo* methods as well as *in vitro* methods.

Guidance provide and presence of working examples in the specification

Despite a tremendous amount of effort by skilled artisans in the field of gene delivery and expression *in vivo*, there remain significant hurdles known in the art to make and use the invention over the scope claimed. Anderson reports that progress in developing effective gene therapy is slow. Anderson further states, "the efficiency of gene transfer and expression inhuman patients is, however, still disappointingly low. . . . [the] goal is more difficult to achieve than many investigators had predicted. . ." See Anderson Nature Vol. 392, supp 1998 page 25, column 1.

Verma et al. and Palu et al. also discuss the inherent difficulties transfecting cells *in vivo* by targeted delivery mechanisms. See Verma et al. Nature Vol. 389 1997 and Palu et al. J. of Biotech. Vol.68 1999. Transferred genes can be induced to function in a whole animal; however, no approach has been fully successful for *in vivo* gene transfer. See Verma, page 239. Moreover, the main obstacle to the development of gene therapy is the targeted long-term expression of the transgene. The *in vivo* transfer of genes to target cells has not been fully successful for many reasons including the complexity the biological systems of living organisms, the inability of the genes to reach enough of the target cells, and the inability of the genes to function properly or for a significant period of time even if they do reach the cells. See Palu, page 10 and Anderson, page 25.

State of the prior art and unpredictability of the art

Applicant has not provided any working examples in the specification toward a method of transferring a nucleic acid encoding a protein of interest to target cell *in vivo*. The disclosure is limited to a general discussion of the peptide-vector use for gene transfer in addition to examples discussing the systhesis of the vector, preparation of marker genes and extraction of mRNA to measure transcription of the marker gene. See Specification, examples, pages 10-13.

Upon examination of Applicant's disclosure, no evidence or data is apparent that the vector will reasonably reach a cell *in vivo*, deliver the DNA to the target cell *in vivo* in a sufficient amount for expression, or express the desired nucleic acid properly. Given the nature of the invention claimed, the unpredictability of the art and the lack of guidance and working examples in the specification, one of skill in the art is unable to use the invention commensurate with the scope claimed without engaging in undue experimentation.

Claims 1-4 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

The word "gene" refers not only to a coding sequence but also to an entire genomic structure. Genomic structure includes introns and all regulatory regions upstream and downstream of coding sequences. The word "gene" represents a broad genus of molecules for which the entire genomic structure of a representative number of eukaryotic "genes" is not known. Therefore, these claims fail to describe the broad genus of genes with such descriptive means to adequately describe the present invention. One of skill in the art could not reasonably conclude that Applicant was in possession of the broad genus of genes claimed at the time of

filing. It is suggested that the word gene be replaced with terminology such as "nucleic acid sequence".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites "a peptide of" SEQ ID NO:1 and "a DNA of" SEQ ID NOs:2 and 3. This claim is vague and indefinite because it is unclear whether the Applicant is claiming a single peptide of SEQ ID NO:1, a single nucleic acid of SEQ ID NOs: 2 and 3, a fragment of SEQ ID NO:1, a nucleic acid fragment of SEQ ID NOs:2 and 3 or the full length of SEQ ID NO: 1 and SEQ ID Nos:2 and 3.

Claim 5 recites the limitations "the peptide" if SEQ ID NO:1 in line 2, "the DNA of" SEQ ID NO:2 in line, 2 and "the DNA of" SEQ ID NO:3 in line 3. There is insufficient antecedent basis for these limitations in the claim.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (571) 272-0768. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday 7:30 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Konstantina Katcheves
Group Art Unit: 1636